We request that the following claims be added to the application:

What is claimed is:

42. A method of producing a water-insoluble high-molecular weight polymeric material that demonstrates hepatocyte specificity from starting compounds that are initially very water-soluble and when said polymeric material is incorporated into a liposomal carrier system directs the targeted delivery of encapsulated pharmaceuticals, diagnostics and therapeutics to the hepatocytes in the liver of a warm-blooded host, comprising:

    a. The synthesis of a polymeric molecule exhibiting hepatocyte specificity comprising the characteristics of

        (a') containing the transition series element chromium; and

        (b') a bio-organic moiety capable of complexing said transition element, wherein an octahedral structure is formed which contains an atom of chromium and two bio-organic moieties that result in the formation of a (bis) chromium complex; and

        (c') the subsequent polymerization of the (bis) chromium complex represented by repeating octahedral structural units resulting in progressively, higher molecular weight multiples of said complex in order to create a water-insoluble polymeric derivative; and is capable of

    b. Being solubilized in organic solvents in conjunction with other lipid constituents in order to achieve a single-step mixing and organic solubilization of all components; and

    c. The subsequent drying of all said components in order to formulate a dried organic composition in which the components are uniformly dispersed; and

    d. dispersing the components in a buffered aqueous phase media accompanied by energy input to form a uniform suspension of liposomes wherein the hepatocyte specific polymeric (bis) chromium complex is uniformly dispersed in the hydrocarbon region of the bipolar liposomal membrane.

43. The method of Claim #42, wherein said polymeric (bis) chromium complex is prepared by a synthesis comprising:

    a. combining an aqueous solution of N-2,6,-diisopropylphenylcarbamoylmethyl iminodiacetic acid maintained within a pH range between 3.2 and 3.3 with an

aqueous solution of a chromium compound maintained within a pH range between 4.0 and 4.4 to form a reaction solution; and

b. maintaining the reaction solution at a pH between 3.2 and 3.3 to form the (bis)chromium complex of Claim #42; and

c. incubating said complex in aqueous media for several days at ambient temperature to form a high molecular weight bio-organic polymer with identical repeating octahedral structural units containing chromium that are connected by hydroxyl bridging groups wherein said complex in a time-dependent process precipitates from solution and demonstrates insolubility in aqueous media which is counterbalanced by a new solubility preference for organic solvents and said complex provides targeting capability specific for liver hepatocytes.

44. The process of combining the product of Claim #43c with selected lipid constituents in the presence of organic solvents to form *in situ* organic solution of all components using a single-step addition procedure; and

a. drying the components under vacuum to create a dried mixture of said polymer and said lipid constituents in which all organic components are uniformly and homogeneously mixed; and

b. adding a physiologically compatible aqueous phase buffer to said dried mixture and then introducing an energy factor to uniformly disperse said organic components in the aqueous phase media which results in the formation of liposomes that demonstrate hepatocyte specificity.

45. The process of Claim #44, which further includes the incorporation of a pharmacological, diagnostic, or therapeutic agent in the targeted liposomal hepatocyte specific delivery system.

46. The specific targeted delivery system of Claim #45, wherein said pharmacological, diagnostic or therapeutic agent is sequestered by the liposomal matrix or entrapped in the liposomal core volume or associated with the liposomal surface or is otherwise captured by the liposome through the utilization of various combinations of these sequestering means.

47. The specific targeted delivery system of Claim #46 wherein said pharmacological agent comprises insulin or a derivative thereof.

48. The specific targeted delivery system of Claim # 46 wherein said pharmacological agent comprises serotonin or a serotoninergic agent.

49. The specific targeted delivery system of Claim # 46 wherein said pharmacological agent comprises interferon or other antiviral agent.

50. The specific targeted delivery system of Claim # 46 wherein said liposomal matrix comprises 1,2-distearoyl-sn-glycero-3-phosphocholine, cholesterol, dicetylphosphate and the polymeric targeting molecule.

51. The targeted delivery system of Claim # 50, wherein said pharmacological agent is selected from insulin or an insulin derivative, or serotonin, or a serotonin derivative that contains biologically active serotoninergic properties wherein said biologically active agents may be used singly or in various combinations to achieve a therapeutic benefit.

52. A hepatocyte specific targeted delivery system, comprising

    a. a bipolar liposomal membrane structure; and

    b. a water-insoluble polymeric (bis) chromium complex containing at least one atom of chromium and one or more than one of said bio-organic moieties, wherein the polymeric structure of the hepatocyte targeting molecule has undergone *in situ* chemical exchange reactions producing from the parent polymer a mixture of dissociated moieties wherein said dissociated moiety exists with or without metal in the liposomal membrane.

53. The dissociated moiety of claim # 52b wherein said moiety is N-(2,6-diisopropylphenylcarbamoylmethyl)iminodiacetic acid.

54. The hepatocyte specific targeted delivery system of Claim # 53 wherein said liposomal membrane comprises a mixture of 1,2-distearoyl-*sn*-glycero-3-phosphocholine, cholesterol, and dicetylphosphate and a mixture of the foregoing lipids.

55. The hepatocyte specific targeted delivery system of Claim # 53 wherein said 1,2-distearoyl-*sn*-glycero-3-phosphocholine is present in an amount of about 25.5 micro moles/ml, said cholesterol is present an amount of about 6.85 micro moles/ml and said dicetylphosphate is present in an amount of about 0.465 micro moles/ml.

Sincerely,

W. Blair Geho, M.D., Ph.D.
Chairman and CEO